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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,238	10/21/2005	Jan Henrik Ardenkjaer-Larsen	PS0267	8175

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
10/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,238	ARDENKJAER-LARSEN ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/23/2009 has been entered.

Status of Claims

Claims 1-12 have been cancelled. Claims 13-18 are newly added and are examined herein on the merits for patentability.

Response to Arguments

Any rejection not reiterated herein has been WITHDRAWN as being overcome by amendment.

Applicant's arguments filed 7/23/2009 have been fully considered but they are not persuasive, for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons set forth in the previous Office Action.

Applicant argues on pages 5-6 of the Response that the specification set forth that "the hydrogenatable substrate used may be a material such as a para-hydrogenation substrate as discussed in WO 99/24080. For in vitro or in vivo MR studies of biological or quasi-biological processes or synthetic polymer (e.g. peptide, polynucleic acid etc.) syntheses, the substrate is preferably hydrogenatable to form a molecule participating in such reactions, e.g. an amino acid, a nucleic acid, a receptor binding molecule, etc. either as a natural such molecule or an analog." Applicant asserts that in the context of the claimed invention, one of skill in the art would understand what is meant by a "hydrogenatable, unsaturated compound" as the terms "hydrogenatable" and "unsaturated" are terms in the art, and that furthermore the Specification references published document WO 99/24080 and its U.S. equivalent, US 6,574,495 for examples of suitable hydrogenatable, unsaturated compounds.

This is not found to be persuasive. There is no description of the claimed hydrogenatable, unsaturated substrate compound required to make and use the contrast agent broadly claimed. There is no description provided regarding what type of

specific chemical moieties are used to represent the substrate that would render such a compound to be useful as a contrast agent. There is very little predictability in the art concerning any undefined species which may represent a substrate compound and which chemical moiety would represent a substrate out of an almost unlimited number of chemical species which may be possible. The specification does not provide guidance to the specific identity or physical/chemical structure of the variables which represent a substrate, other than a few examples such as amino acid, nucleotide, and because the structures of these elements are undefined, it is unclear how Applicant envisaged suitable elements to satisfy the functional requirements of the substrate. Accordingly, the claims are more broad than the disclosure provides guidance for, and the metes and bounds of which types of unsaturated compounds may be suitable for use as hydrogenatable substrate for use in producing MR contrast agent are not clearly set forth. It is noted that Applicant refers in the specification as amended to substrates "as discussed in WO 99/24080 or its U.S. equivalent, United States Patent No. 6,574,495." However, an incorporation by reference must express a clear intent to incorporate by reference by using the words "incorporate" and "reference" (see 37 CFR 1.57(b)). In the instant case, no such statement exists, and thus there is no clear intent to incorporate by reference the subject matter that identifies a hydrogenatable, unsaturated substrate compound, and no adequate description of such a compound has been provided. A description of the identity of a suitable substrate compound is considered to be essential material to the method which is claimed.

New Grounds for Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Barkenmeyer et al. (*J. Magnetic Resonance*, 1996, p. 129-132).

Barkenmeyer discloses that in a 400 MHz Varian spectrometer (VXR-400), parahydrogen was enriched to about 50% by passing ordinary hydrogen over charcoal in a U-tube cooled to 77 K in liquid nitrogen. This gas was bubbled into a solution, containing 3.1 ml CDC13, 20 mg of the catalyst [Rh(norbomadiene)(PPh_3)$_2$], and 100 μl of l-hexyne or phenylacetylene. Samples were subjected to six pulse sequences. The field of the spectrometer would be a stationary magnetic field, and the pulses read on on pulses of magnetic field having a different orientation to the pulse prior, as claimed. Enhanced ^{13}C spectra are recorded. See pages 129-131. See especially pulse sequences, on page 130, Figure 1 (e.g. 90 degree, 180 degree pulses, etc.). It is noted that the recitation of the intended use of the hydrogenated substrate as a contrast agent has not been given patentable weight to distinguish over Barkenmeyer because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the

intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Barkenmeyer discloses the same method steps as those that are claimed, Barkenmeyer meets the claims.

Claims 13-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Golman *et al.* (WO 99/24080, whereby US 6,574,495 is relied upon as equivalent).

Golman discloses methods of magnetic resonance investigation of a sample which relies on ex vivo nuclear polarization of a selected non-hydrogen, non-zero imaging nuclei (e.g. ^{13}C), of an MR imaging agent by reaction of a precursor with para-hydrogen enriched hydrogen gas. The method comprises (i) reacting para-hydrogen enriched hydrogen with a hydrogenatable MR imgaging agent precursor containing a non-hydrogen non-zero nuclear spin nucleus to produce a hydrogenated MR imaging agent; (ii) administering said hydrogenated MR imaging agent to said sample; (iii) exposing said sample to radiation of a frequency selected to excite nuclear spin transitions of said non-zero nuclear spin nucleus in said hydrogenated MR imaging agent; (iv) detecting magnetic resonance signals of said non-zero nuclear spin nucleus from said sample (column 2, lines 25 – 55). The hydrogenation step preferably is performed in liquid or gaseous phase, in the presence of catalyst (column 3, lines 35 – 40). MR imaging precursors are hydrogenatable and preferably include one or more unsaturated bond (column 4, lines 21 – 24). It is desirable to carry out the hydrogenation step in a very low magnetic field (column 13, lines 1 - 15). One the MR imaging agent has been administered, chosen procedures for detecting MR signals are

that which is well known from conventional MR scanning. Such conventional MR scanning includes a primary magnetic and RF pulses. When the MR signal derives from hyperpolarization of the reporter nuclei, the signal must be recovered following a train of 180° RF pulses (column 19, lines 5 – 20). With regard to instant claim 3, Golman teaches that the Larmor frequency of carbon is about 10 MHz at 1 T, and thus the rf-absorption in a patient is less than in ^{1}H imaging (column 17, lines 45 – 50). Golman teaches various pulse sequences having pulses in different orientation (e.g. pulse 180, 90, waiting for t/2, etc.). See column 19 – 20. It is noted that Golman teaches steps in addition to those claimed, e.g. administration to patient before exposure to radiation of a frequency to excite nuclear spin transitions, etc. However, the comprising language of the instant claims does not preclude the presence of additional steps, accordingly Golman meets the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites the limitation "the constant magnetic field" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 10/526,134. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of preparation of an MR contrast agent comprising obtaining a solution comprising a solvent, a hydrogenatable, unsaturated substrate compound comprising imaging nuclei, hydrogenating with para-hydrogen enriched hydrogen gas, and exposing said hydrogenated contrast agent to a magnetic field. In the '134 Application, the magnetic field is a combination of a stationary magnetic field and an oscillating magnetic field. Dependent claims of the '134 Application define that the exposure to oscillating magnetic field in combination

with stationary magnetic field comprises exposing the contrast agent to at least one series of pulses of the oscillating magnetic field, including pulses having differing orientation (e.g. 180 degrees, 90 degrees, etc.) (see claims 6-10). The claims of the instant Application require exposing the contrast agent to an initial magnetic field having an initial orientation followed by a series of magnetic field pulses for enabling spin-order transfer, wherein each pulse has a different orientation to the pulse prior. Accordingly, the claims are overlapping in scope and are obvious variants of one another.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS